

The University of Chicago

SUBSTITUTION
REACTIONS OF DERIVATIVES OF
NITROBENZENE

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1935

By
YIH-TONG KU

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A study of substitution reactions of para-nitrodimethylaniline, para-nitroanisole, para-nitrochlorobenzene and para-nitrobromobenzene was carried out at the suggestion and under the guidance of Professor Stieglitz to obtain more evidence in the general problem of substitution in the aromatic series. Previous investigation in this laboratory¹ had been primarily concerned with substitution in the derivatives C_6H_5X , in which X represents ortho-para directing groups. In the present study, a meta directing group NO_2 was incorporated in the molecule with a view to ascertaining its influence from the point of view of the Stieglitz theory of substitution in the aromatic compounds,² and in particular to throw further light on some of the more remote problems connected with the theory.³

¹I. E. Muskat, Doctorate Dissertation, University of Chicago, 1927; Abstracts of Theses, Science Series, University of Chicago, V, 217.

F. C. M. Smithson, Doctorate Dissertation, University of Chicago, 1930.

J. J. Hoffman, Doctorate Dissertation, University of Chicago, 1931.

²J. Am. Chem. Soc., 44, 1293 (1922).

³Unpublished report by Stieglitz and Muskat.

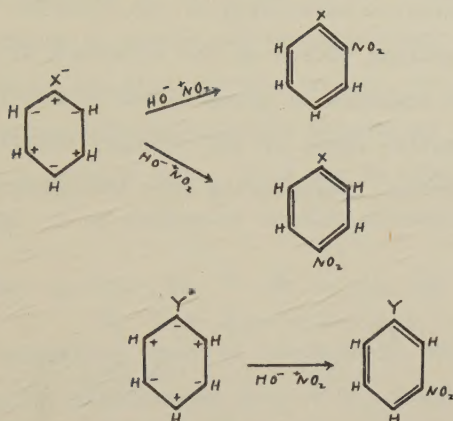
I. INTRODUCTION

The Stieglitz theory¹ of substitution in the aromatic nucleus is based on the following main considerations: (1) The guiding forces determining the position to which a substituent will go, are primarily electrical fields of force² resulting from the positions of valence electrons. (2) These electrical forces are exerted through the double bonds of the Kekulé structure for benzene and its analogs. (3) The relative polarity of the ends of these double bonds is determined by the electrical character of the substituting groups X and Y, in the compounds C_6H_5X and C_6H_5Y .³ When X is a negative group ($\bar{O}H$, $\bar{N}H_2$, $\bar{O}CH_3$, $\bar{N}(CH_3)_2$, Cl^- , Br^- , etc.), the ends of the double bonds in positions 2, 4 and 6 are relatively negative; when Y is a positive radical ($\dot{N}O_2$, $\dot{S}O_3H$, $\dot{C}OOH$, $\dot{C}N$, $\dot{C}HO$, etc.) positions 3 and 5 are relatively negative. Substitution always occurs at the negative valence ends, by combination with positive components (Cl^+ , Br^+ , $\dot{N}O_2$, $\dot{S}O_3H$, etc.). As a result, the C_6H_5X with a negative X, yield ortho, ortho, para substitution products, and the C_6H_5Y series with a positive Y, yield meta, meta derivatives.

¹Loc. cit.

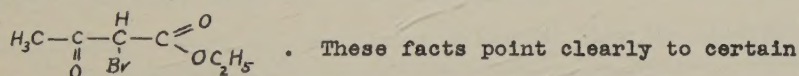
²Stereo-chemical interferences may prevent substitution.

³Cf. Fry, Z.f. physik. Chemie, 76, 385 (1911), on the Electrical Character of X and Y.



The actual mechanism of the substitution is considered comparable with that of substitution in such aliphatic compounds as acetoacetic ester, and its many analogs.¹ Acetoacetic ester itself shows many of the fundamental characteristics of a phenol and may be considered to be an aliphatic phenol. It will be recalled that of the tautomeric forms of the ester, only the

enol-form
$$\text{H}_3\text{C}-\underset{\text{OH}}{\underset{|}{\text{C}}}=\overset{\text{H}}{\text{C}}-\overset{\text{O}}{\underset{|}{\text{C}}}-\text{OC}_2\text{H}_5$$
 reacts,² for instance with bromine, to produce a substitution product of the keto-form,³



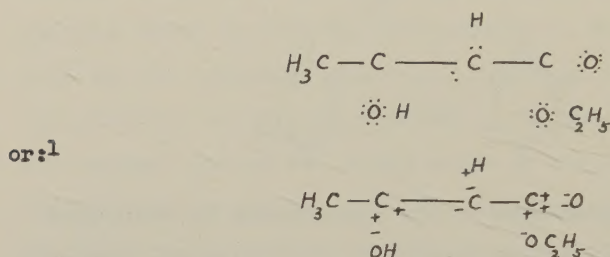
fundamental characteristics of the substitution reaction. In the enol form of the ester, the end of the ethylene double bond in the α -position is relatively negative: this is evident from

¹These include aldehydes, ketones, esters, nitriles, etc.

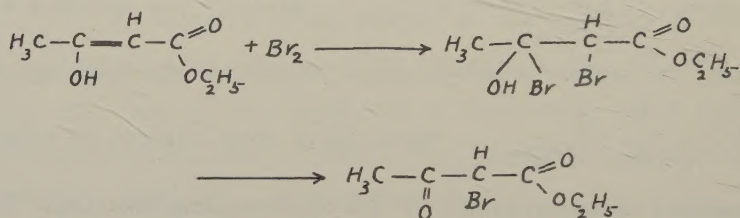
²The structure
$$\text{H}_3\text{C}-\underset{\text{OH}}{\underset{|}{\text{C}}}=\overset{\text{H}}{\text{C}}-\overset{\text{O}}{\underset{|}{\text{C}}}-\text{OC}_2\text{H}_5$$
 resembles the aromatic nucleus also in showing the α -carbon atom as a central atom of a system of conjugated double bonds.

³Kurt H. Meyer, Ann. 398, 51, 66 (1913); Ber. 54, 2265 (1921).

the fact that in the ketonisation of the enol, H^+ goes back to the α -position. The relative negativity of the α -carbon results most likely from the repelling effect on the electrons of the double bond exerted by the negative OH group in the β -position, supplemented by the attractive force of the strongly positive carbon atom of the ester group. Emphasizing only the essential electric forces we have:



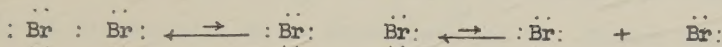
In the formation of α -bromacetoacetic ester from this enol form, it is usually assumed that the molecule of bromine is added to the enol double bond and that hydrogen bromide is then lost:



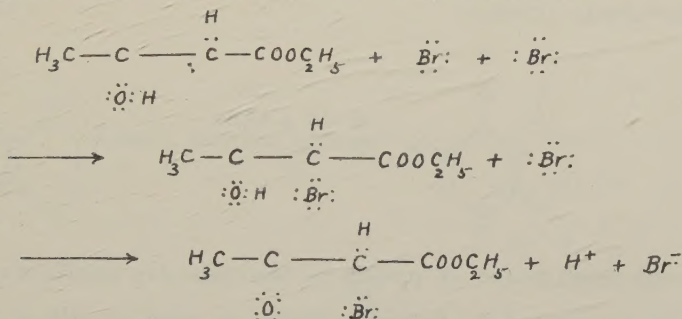
It is quite possible that the addition of bromine to the double bond is thus first completed and then by the loss of hydrogen

¹The signs + and - indicate simply that the pair of electrons forming the bond is closer on the average to the atom carrying the - sign than to the atom carrying the + sign, i.e., that the field around C^- is relatively negative, that around C^+ is relatively positive. There is no complete transfer of electrons as in the case of ionogens.

bromide, a new unsaturated group $C=O$ is produced.¹ But simultaneous addition of two atoms to two other atoms is an improbable course of action and an unnecessary assumption.² From the structure of the final product we are justified in considering only that the unsaturated negative valence of the double bond has absorbed a bromine atom. This may be absorbed as the positive component $\ddot{Br}:$ of an activated bromine molecule:



Electrical neutrality would be restored in the ester molecule by the practically simultaneous loss of H^+ , repelled as it would be by the positive charge developed on the β -carbon atom:



Interaction of the negative α -carbon atom with the whole bromine molecule $:\ddot{Br}: \ddot{Br}:$ with the loss of $:\ddot{Br}:$ is a similar possibility. There is some direct evidence³ that the absorption

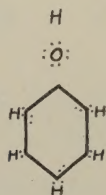
¹There are any number of organic reactions in which saturation of a double bond is followed by the reversion to an unsaturated molecule. In some instances the intermediate saturated compounds have been isolated--as in the formation of aldol, $H_3C-CHOH-CH_2CHO$, from acetaldehyde, and the subsequent transformation of aldol into cretonaldehyde, $H_3C-CH=CH-CHO$. It is quite possible, and perhaps probable, however, that in many other cases, only partial saturation, as described in the text, precedes the formation of the new unsaturated compound.

²Stieglitz, *J. Am. Chem. Soc.*, 44, 1304 (1922).
Unpublished report by Stieglitz and Muskat.

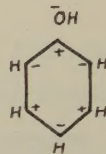
³E. Terry and Eichelberger, *J. Am. Chem. Soc.*, 47, 1067 (1925).
Francis, *J. Am. Chem. Soc.*, 47, 2347 (1925).

of $\text{Br}\cdot$ takes place after absorption of $\text{Br}\cdot$ by olefines, since in the presence of chloride ions the addition product is to a considerable extent a bromine chloride, $\text{R}_2\text{C} - \text{C} \text{R}_2$, rather than
 $\begin{array}{c} \text{Cl} \quad \text{Br} \end{array}$
 a dibromide.

The Stieglitz theory of substitution in aromatic compounds assumes a mechanism which follows in general the course outlined for the substitution of bromine in acetoacetic ester, an aliphatic phenol. We may use phenol as an illustration of the $\text{C}_6\text{H}_5\text{X}$ series favoring substitution in the ortho, ortho and para position. The negative hydroxyl group, by repelling the more mobile electron pairs of the Kekulé double bonds, leads to the electronic formula:



or in a more easily scanned form,¹

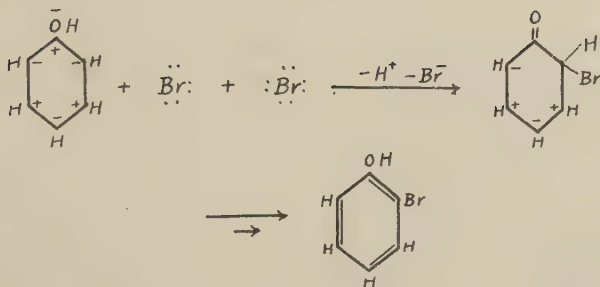


Ortho bromination of phenol in the negative positions 2 and 6 is considered to follow exactly the same course as in the bromination of acetoacetic ester, ketone forms of bromophenols² being the first products formed, and then changing to the more stable phenolic forms:³

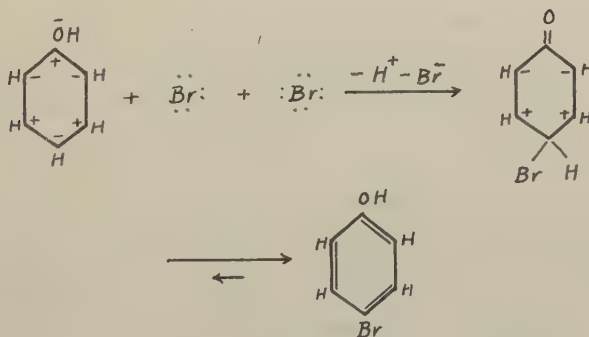
¹See the footnote on page 4. The - signs indicate that the electrons of the three double bonds are displaced toward the 2, 4, 6 carbon atoms, the + signs that carbon atoms 1, 3, 5 are relatively positive.

²J. Am. Chem. Soc., 44, 1303 (1922).

³Only the essential steps are indicated.

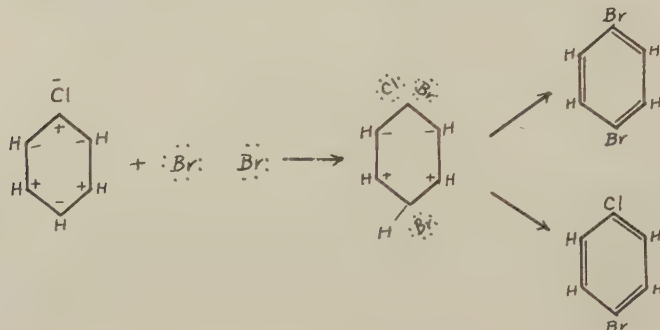


Bromination in the negative para position follows a like course, corresponding to the 1,4 addition reactions of conjugated double bond systems:



A question of special importance is at once met: Is addition of two bromine atoms (Br_2) to the 1,2 or the 1,4 carbon atoms at all consummated before the loss of the hydrogen bromide, or is Br^+ added only to the negative carbon atoms 2, 4, or 6, H^+ being lost simultaneously from the OH group to restore the electrical neutrality of the molecule, in the way discussed for acetoacetic ester? Similarly, is there complete saturation before a reversion to a new condition of unsaturation in such

substitution reactions as bromination by bromine, chlorination by hypochlorous acid, nitration by nitrous or nitric acid, etc.? Investigation of this phase of the problem has been carried out, for instance, in the formation of para substitution compounds. Complete addition would proceed as follows:¹



It is clear that the complete addition of bromine in the bromination of chlorobenzene would lead to the possibility of reversion to an unsaturated condition by the loss of hydrogen chloride by some of the molecules, and of hydrogen bromide by the rest of them. That would evidently result in the formation of some dibromobenzene by the loss of hydrogen chloride, and of chlorobromobenzene, by the loss of hydrogen bromide. The experimental study of the action² showed that hydrogen bromide alone is formed together with chlorobromobenzene. This result indicates clearly that complete addition of bromine has not occurred.

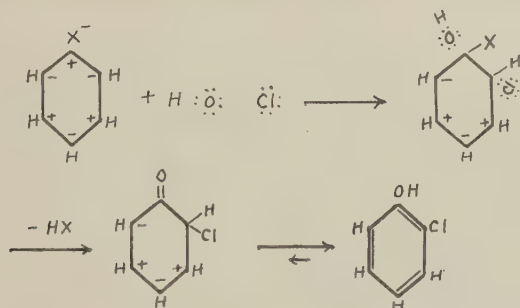
In the action³ of strong aqueous hypochlorous acid on bromobenzene and chlorobenzene, opportunity for the loss of halogen acid and the formation of chlorinated phenols would follow

¹Cf. Muskat and Stieglitz, Doctorate Dissertation of I. E. Muskat, loc. cit.

²Ibid., p. 41.

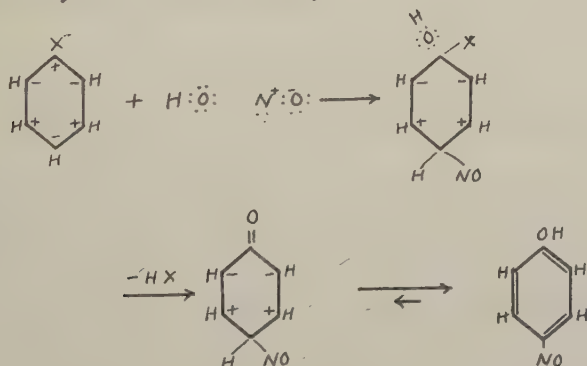
³Ibid., p. 45.

from complete addition. For instance in ortho substitution:



Color indications of chlorophenols were obtained, but not enough of the compounds to isolate an acyl derivative.

On the other hand, the action of hypochlorous acid on dialkyl anilines, triphenyl amine, etc.,¹ and especially of nitrous acid on phenolic ethers,² brought definite proof of complete addition of the reagent at least to some extent. Phenolic derivatives were isolated and fully identified by being converted into their esters. For X=OCH₃, OC₆H₅, N(CH₃)₂, etc., we have, for instance, with nitrous acid,



The greatest proportion of phenol derivatives (up to 55%) was

¹F. C. M. Smithson, Doctorate Dissertation, University of Chicago, 1930.

²J. J. Hoffman, Doctorate Dissertation, University of Chicago, 1931.

obtained by Hoffman¹ in a study of the action of nitrous acid on anisol.

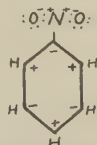
From these results we may draw the important conclusion that complete saturation of a Kekulé double bond in the benzene nucleus does not as a rule accompany substitution in ortho and para positions. However, it has now been proved that saturation does occur occasionally to a lesser or greater extent and that substitution occurs in the same positions under the same conditions in either type of cases. It is a fair conclusion that in both cases, substitution starts in the same way, namely, by the absorption of a positive addendum (Cl^+ , Br^+ , NO^+ , etc.) by the relatively negative ends of the Kekulé double bonds in the nucleus (ortho and para positions). As a rule, electric and structural equilibrium seems to be re-established by the immediate loss of H^+ , the system returning thus again to the ordinary condition of the benzene nucleus.² The most loosely held H^+ will be lost, from :O: H in the case of a phenol, an intermediate ketone form of a substituted phenol resulting, from :N: H in the case of an aniline derivative, from C: H if there is no other H available. To some extent, depending on the characteristics of X and of the reagent used, the theoretical possible addition is consummated, revealing itself by the nature of the secondary products obtained. This is in the aromatic series essentially the same process as is observed in a number of instances in the aliphatic series.

It has remained desirable to study in a similar manner

¹Ibid., p. 8.

²Stieglitz, J. Am. Chem. Soc., 44, 1304 (1922).
Unpublished paper by Stieglitz and Muskat.

the course of action in the presence of a positive group Y in C_6H_5Y , which would strongly favor meta substitution. The nitro group (NO_2) is such a group. By virtue of the attraction of the positive radical for the mobile electrons of the Kekulé double bonds, it makes positions 1, 3 and 5 relatively negative:

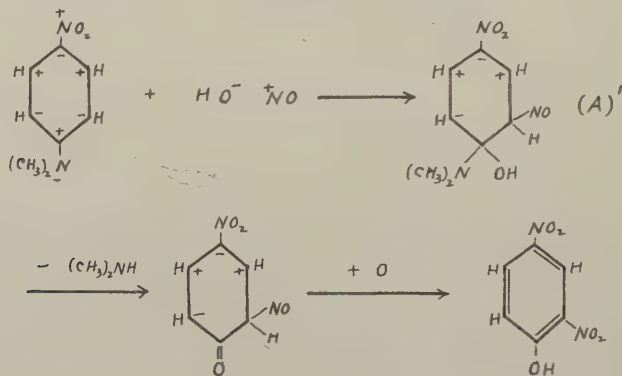


To secure evidence of any complete addition to a double bond, it was necessary to introduce in position 2 or 4 an X group which would be removable if complete saturation should occur in any stage of the substitution reaction. Such groups are $\bar{N}(CH_3)_2$, $\bar{OR}$, $\bar{Cl}$, etc., according to Stieglitz and his collaborators.¹ Their effect on the electron pairs would place the relatively negative ends in positions 3 and 5 and thus they would supplement the effect of the nitro group in position 1. For this reason the investigation of the action of nitric acid, nitrous acid and hypochlorous acid on para-nitrodimethyl aniline, on para-nitroanisole, para-nitrochlorobenzene, and para-nitrobromobenzene was undertaken. A special objective was also that of determining whether the introduction of the nitro group had any favorable or unfavorable action in the matter of completion of saturation as compared with the non-nitrated derivatives of the same type previously examined by Stieglitz and his collaborators.

¹I. E. Muskat, loc. cit.
 F. C. M. Smithson, loc. cit.
 J. J. Hoffman, loc. cit.

II. DISCUSSION OF RESULTS

In the study of the action of nitrous acid on para-nitrodimethylaniline, four different solvents were tried,--glacial acetic acid, dilute hydrochloric acid, dilute sulfuric acid, and chloroform. All gave results leading to the same conclusion that complete saturation of the Kekulé double bond at the 3,4 position does occur, but probably only to a very small degree. The evidence for this is found in the formation of small quantities of 2,4-dinitrophenol which would be produced as follows:



When dilute sulfuric acid or chloroform was used as the solvent, 2,4-dinitrophenol was isolated, though only in small quantities. It was identified in the form of its benzoic acid

¹The addition product A could also lose water and (after oxidation of NO to NO₂) thus produce 2,4-dinitrodimethylaniline. We shall find that the latter is another product of the action, formed in large quantity. The very small proportion of dinitrophenol formed is taken to indicate that 2,4-dinitrodimethylaniline is produced chiefly by uni-polar absorption of NO in position 3 (see p. 13).

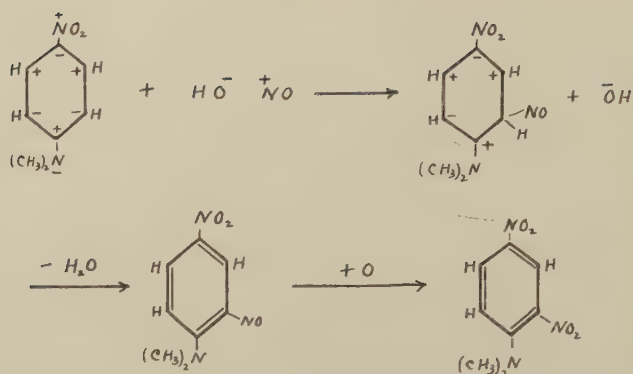
ester by the melting point of the ester mixed with benzoic acid ester of known 2,4-dinitrophenol. In the other two cases, where glacial acetic acid or dilute hydrochloric acid was used as the solvent, the 2,4-dinitrophenol was not isolated, but the color reaction of the nitrophenol was obtained. The fact that 2,4-dinitrophenol was isolated rather than 2-nitroso-4-nitrophenol, is undoubtedly due to the readiness with which the latter is oxidized by nitrous acid; a similar fact was described and discussed in the investigation of the action of nitrous acid on anisol and diphenyl ether¹ by Stieglitz and Hoffman.

Since 2-nitroso-4-nitrodimethylaniline would be oxidized likewise to 2,4-dinitrodimethylaniline, it was necessary to avoid obtaining dinitrophenol by saponification of the dinitrodimethylaniline.² Special precautions were taken which were based on a study of synthetic 2,4-dinitrodimethylaniline. The procedure used is described in the experimental part of this report, p. 31.

2,4-Dinitrodimethylaniline was isolated and identified as a second product of the action of nitrous acid on p-nitrodimethylaniline. It is formed in small quantities (less than 10%) when dilute sulfuric acid was used as the solvent, and as the major product when chloroform was used as the solvent. It might be produced by the loss of water from the addition product A, as indicated above. But the formation of only traces of dinitrophenol by the decomposition of A in acid solution with the loss of dimethylaniline, clearly indicated the formation of 2,4-dinitrodimethylaniline is due rather to a primary uni-polar addition of NO^+ to position 2. This is shown as follows:

¹Hoffman, loc. cit., p. 8.

²Cf. K. H. Mertens, Ber., 19, 2124 (1886).



Rather unexpectedly, the chief product obtained by the action of nitrous acid on p-nitrodimethylaniline in glacial acetic acid solution to which a few cc. of concentrated hydrochloric acid was added, was N-nitroso-p-nitromonomethylaniline, the yield being above 90%. This compound was identified by its melting point, by analysis, and by chemical reactions which included the nitrosamine reaction¹ and the decomposition to p-nitromonomethylaniline.² N-nitroso-p-nitromonomethylaniline had been obtained by the action³ of nitrous acid on p-nitrosodimethylaniline in hydrochloric acid solution, but it was reported that nitrous acid failed to react with p-nitrodimethylaniline under the similar conditions.

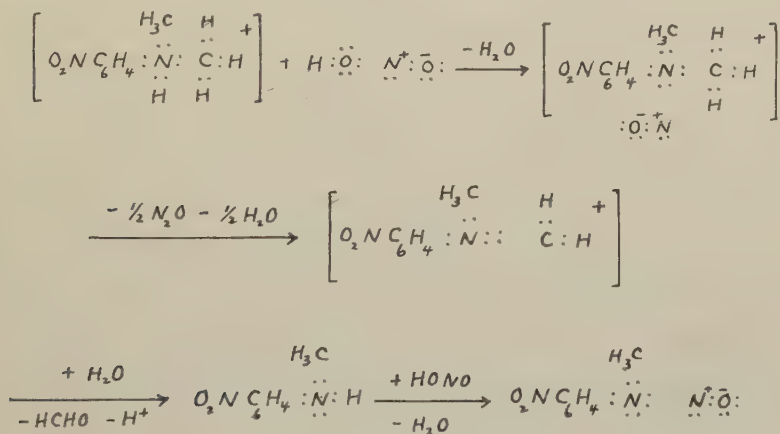
However, in this study of the action of nitrous acid on p-nitrodimethylaniline in dilute hydrochloric acid (approximately 6-N), it was found that N-nitroso-p-nitromonomethylaniline was again the chief product isolated. A very small amount of 2,4-dinitrophenol was also obtained, too small in quantity for the

¹Cf. Mulliken, "Identification of Pure Organic Compounds," II, 27.

²Stoermer and Hoffmann, Ber., 31, 2528 (1898).

³Hodgson and Smith, J. Chem. Soc., (1931), 1509.

preparation of a derivative; it was partially identified by the color reaction. In Further experiments, under varying periods of reaction, and with varying acid concentrations, N-nitroso-p-nitromonomethylaniline was always the chief product isolated. Another somewhat similar case was then found in the literature, namely that in the action of nitrous acid on p-bromodimethylaniline in hydrochloric acid solution, N-nitroso-p-bromomonomethylaniline¹ was one of the products obtained. A mechanism for the conversion of p-nitrodimethylaniline into N-nitroso-p-nitromonomethylaniline has been suggested by Professor Stieglitz as follows:



This diagram represents the following series of reactions of a simple character: (a) p-nitrodimethylaniline is converted into its salt ion by absorbing H^+ in the acid solution (see p. 17) and this ion is converted into a nitroso derivative by the ordinary replacement of H^+ in NH compounds by NO ; (b) the nitroso compound undergoes an intramolecular oxidation-reduction, the methyl group being oxidized to a methylene group CH_2 . This

¹Würster and Scheibe, Ber., 12, 1816 (1879).

reaction is comparable with the formation of benzonitrile from benzaldoxime and with the oxidation of an adjoining methyl group by $\text{Cl}^\cdot$, the hypochlorous radical, in N-chloroalkylamines; (c) the formaldehyde derivative thus produced is hydrolyzed with the elimination of formaldehyde and (d) the resulting methylnitraniline is converted into its nitrosoamine, the final product, in the usual fashions. The presence of formaldehyde was proved by the resorcinol test¹ and by the guaiacol ring test.²

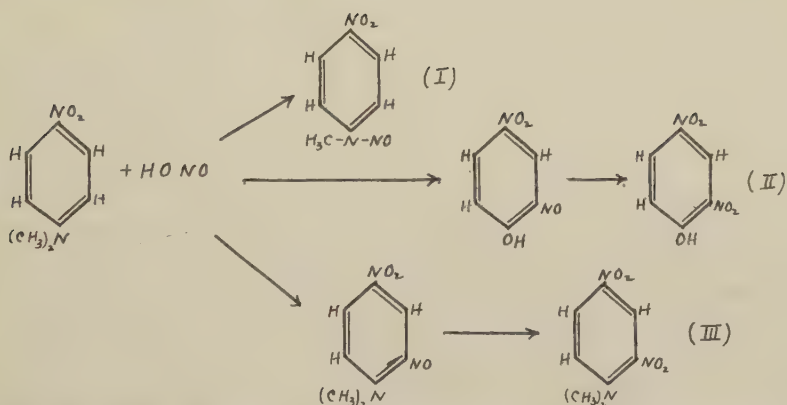
In order to be sure that the reaction takes place in any strong acid solution, and in an attempt to obtain the dinitrophenol in a larger yield and purer form, dilute sulfuric acid (approximately 6-N) was next used as a solvent. N-nitroso-p-nitromonomethylaniline was again the chief product isolated (about 90%); 2,4-dinitrodimethylaniline in less than 10%; and 2,4-dinitrophenol was obtained in a purer and slightly larger quantity, so that the conversion of it to the benzoic acid ester was made possible. The production of 2,4-dinitrophenol in the reaction was thus definitely proved and the complete saturation of the Kekulé double bond at the 3,4 position (the NO_2 group occupying position 1), fully established. It is also quite evident that the reaction of complete saturation is a minor one.

It is a significant fact, that we have thus three reactions occurring at the same time: substitution in an extranuclear group; substitution in the nucleus through complete saturation of one of the Kekulé double bonds; and substitution in the nucleus through absorption of a positive group by the negative end only of the Kekulé double bond. These reactions may

¹Lebbin, Centralblatt, 1897 I, 270. Also, Rosenthaler, "Nachweis organischer Verbindungen," p.

²H. Meyer, "Nachweis und Bestimmung organische Verbindungen," II, 47.

be summarized as follows:



(I) is the chief reaction (approximately 90%); (II) takes only to a very small extent and (III) to an extent less than 10%.

The N-nitroso-p-nitromethylaniline was found to be a rather stable compound; it did not rearrange to 2-nitroso-4-nitro- (or 2,4-dinitro-) monomethylaniline, even when heated in hydrochloric acid solution. It was hydrolyzed and formed p-nitromonomethylaniline.¹ The formation of N-nitroso-p-nitromonomethylaniline in strong acid solutions as the chief product of the action of nitrous acid on p-nitrodimethylaniline is simply due to the great ease with which an NH group gives a nitroso derivative N-NO, the H⁺ attached to nitrogen representing the most reactive component in the molecule.² The formation of an extra-nuclear substitution here is thus the natural result of an attack on the most reactive group in the molecular system,

¹Loc. cit.

²It is for exactly this reason that acetanilide and other aniline derivatives containing the NH group form first extra-nuclear derivatives, NCl, NBr, N-NO, etc. They are less stable than nuclear derivatives and easily go over into these but they are by no means essential intermediates in the formation of nuclear derivatives.

and is not to be considered a necessary intermediate compound¹ leading to another compound with substitution in the aromatic nucleus.

The action of nitrous acid on p-nitrodimethylaniline in chloroform as solvent gives further evidence that extra-nuclear substitution is not a necessary step prior to nuclear substitution, confirming completely the argument just presented. In the absence of an excess of strong acid, when chloroform was used as the solvent, no extra-nuclear substitution product was isolated; 2,4-dinitrophenol, the nuclear substitution product formed through complete saturation of the Kekulé double bond was obtained in small quantity; and 2,4-dinitrodimethylaniline, the nuclear substitution product probably produced chiefly, if not wholly, through absorption of a positive group by the negative end of the Kekulé double bond, was the major product. The formation of the salt ion of the p-nitrodimethylaniline is the essential step (see p. 15) for the attack by nitrous acid on the extra-nuclear group. In the absence of the necessary acid which could yield H^+ to the amine and convert it in its ion (hydrochloric acid was added dropwise to a suspension of solid sodium nitrite in the chloroform solution of p-nitrodimethylaniline), N-nitroso-p-nitromonomethylaniline was completely absent in the reaction product.

In this study of the action of nitrous acid on p-nitrodimethylaniline, special care has been taken in order to be sure that the 2,4-dinitrophenol was not formed through some other secondary reactions, other than the process of complete

¹Chattaway and Orton, Ber., 32, 3573 (1899); J. Chem. Soc., 77, 134, 789 (1900).
Auwers and Michaelis, Ber., 47, 1275 (1914).
Van Alphen, Rec. trav. chem., 47, 169 (1928).

saturation of a Kekulé double bond. Many blank experiments were carried out and the chemical properties of the other reaction products were carefully studied, with the result that there is no probability at all that the 2,4-dinitrophenol obtained was formed from any source other than that predicted according to the Stieglitz theory of substitution in the benzene nucleus. This result agrees with the findings established by Muskat, Smithson and Hoffman, who started with aromatic amines and ethers containing no meta directing groups attached to the benzene nucleus, whereas in the present study, a strongly meta directing nitro group was attached to the nucleus.

However, a comparison of the relative quantities of 2,4-dinitrophenol isolated in the present study, with the phenols isolated by Muskat, Smithson and Hoffman, leaves no doubt that the introduction of the nitro group is unfavorable to the completion in saturation, although the general process of substitution remains perfectly the same. This unfavorable effect of the nitro group, a matter of degree, not of kind, is probably due to the extremely strong relative negative polarity of the double bond in position 3, the positive nitro group in position 1 adding its effect to that of the negative dimethylamine group in position 4 to make position 3 relatively still more negative. The positive nitroso group of the nitrous acid is thus strongly attracted and will approach position 3 very much more effectively than the negative OH group of the nitrous acid approaches position 4, where the strongly negative dimethylamine group may have a repelling effect on the negative OH group, retarding the latter in reaching the positive end of the 3-4 double bond. There will undoubtedly be other explanations of the unfavorable action of the nitro group toward complete saturation of the Kekulé double bond, but the above unconstrainedly consistent with the theory under investigation.

A study of the action of nitrous acid on p-nitroanisol was next undertaken. However, it was found that p-nitroanisol is very inert toward nitrous acid. The same observation was reported by Hoffman, who used solid p-nitroanisol and a solution of it in carbon tetrachloride.¹

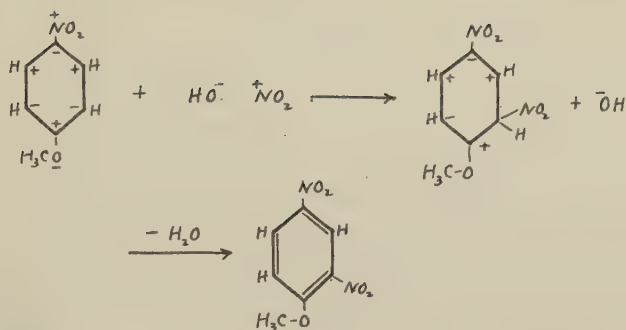
The action of nitric acid on p-nitroanisol was then examined. It was found to differ from anisol, which reacted readily with nitric acid in carbon tetrachloride;² p-nitroanisol is not acted upon by cold concentrated nitric acid or by nitric acid in glacial acetic acid solution at 90°. Concentrated sulfuric acid was finally taken as the solvent.

The action of nitric acid on p-nitroanisol had been studied in 1907 by H. Martinsen³ with the object of determining the different reaction velocities in the nitration of various substituted aromatic compounds. With a different objective, no examination for 2,4-dinitrophenol was made; a good yield of 2,4-dinitroanisol was simply reported. We were able to confirm that finding. According to the Stieglitz theory, 2,4-dinitroanisol is probably formed by uni-polar absorption of the NO₂ in the negative positions 3 and 5 with the almost simultaneous loss of H in these positions. This action is represented by:

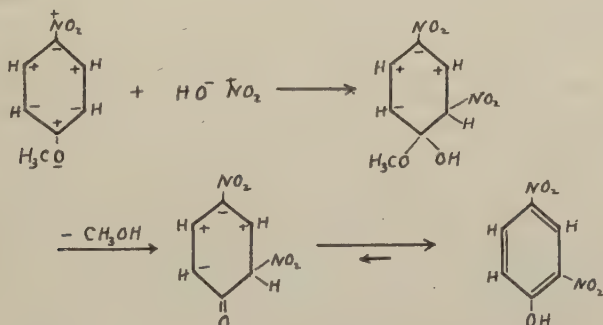
¹Hoffman, loc. cit., p. 25.

²Ibid., p. 28.

³Z. f. Phy. Chem., 59, 617 (1907).



Following the Stieglitz theory, 2,4-dinitrophenol will be one of the products if complete saturation of a Kekulé double bond takes place:



This expectation was fully confirmed. 2,4-Dinitrophenol was isolated and identified as its benzoic acid ester. The possibility of the formation of 2,4-dinitrophenol from any source other than the one described was eliminated through a careful study of the chemical properties of p-nitroanisole and 2,4-dinitroanisole, and by blank experiments.

In line with the results of the action of nitrous acid on p-nitrodimethylaniline, the presence of the strongly meta orientating nitro group together with that of the OCH_3 group, both groups favoring the negativity of position 2 (OCH_3 in position 1), seems again to have effect of diminishing the chance of

complete saturation of the Kekulé double bond. While Hoffman¹ found that "55% of the unrecovered anisol was recovered in the form of p-nitrophenol" by the action of nitrous acid on anisol, only 30 mg of impure 2,4-dinitrophenol was isolated by us from the product of the action of nitric acid on ten grams of p-nitroanisol. Of course, the low yield of the complete saturation product may be due to some other reasons than the effect due to the presence of the first nitro group. By a change of the solvent, the nitrating agent, or the reaction temperature, the quantity of the product formed through complete saturation of the Kekulé double bond might possibly be increased. It is noteworthy that Martinsen,² in the study of the velocity of nitration of 2,4-dinitroanisol by nitric acid, obtained 2,4,6-trinitroanisol exclusively on the one hand, and picric acid exclusively on the other hand, depending simply upon the strength of the sulfuric acid that he used for the preparation of the solution. He showed further that picric acid was not the result of hydrolysis of the anisol by the solvent, but was formed as the result of the action of the nitric acid.

The action of hypochlorous acid on p-nitrodimethylaniline and p-nitroanisol was next taken up in order to determine to what extent, if any, complete saturation takes place, in the presence of meta orientating nitro group. The parallel action of hypochlorous acid on dimethylaniline was investigated by Stieglitz and Smithson,³ and that on anisol by Stieglitz and Muskat.⁴ Both o- and p-chlorophenols were isolated and completely identified

¹Hoffman, loc. cit., p. 8.

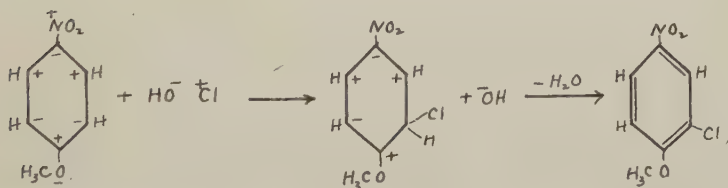
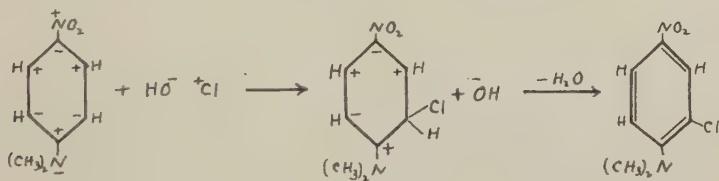
²Z. f. Physik. Chemie, 59, 618 (1907).

³Loc. cit.

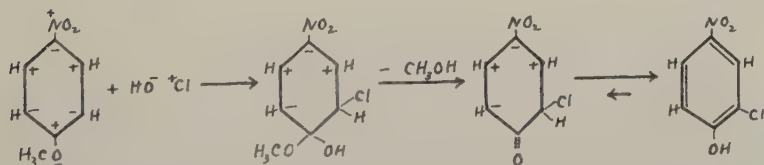
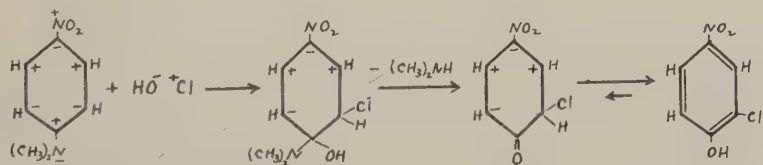
⁴Loc. cit.

in these reactions; their yields did not seem to be so favorable as the yield of p-nitrophenol from anisol and nitrous acid.¹

The action of hypochlorous acid on p-nitrodimethylaniline and p-nitroanisole proved to be a little more complicated than its action on dimethylaniline and anisol respectively. The main compounds isolated indicated only absorption of a positive chlorine atom by the negative end of the Kekulé double bond:



Through complete saturation of the Kekulé double bond, 2-chloro-4-nitrophenol should be formed, at least to some extent:



¹Hoffman, loc. cit.

The 2-chloro-4-nitrophenol, however, would be readily acted on by hypochlorous acid¹ to yield 2,6-dichloro-4-nitrophenol which may be further acted on by more of hypochlorous acid to give higher oxidation products, possibly quinone-like derivatives.² This series of reactions may be responsible for the production of blood-red colored alkaline solutions, formed slowly on neutralizing the acidic solutions, even in a current of hydrogen. The blood-red colored solutions were formed identically in both reactions of hypochlorous acid with p-nitrodimethylaniline and p-nitroanisol, but not in the reaction when nitrous or nitric acid was used in place of the hypochlorous acid. A confirmatory experiment was performed in which the results of the action of hypochlorous acid on 2-chloro-4-nitrodimethylaniline, 2-chloro-4-nitroanisol, synthesized 2-chloro-4-nitrophenol and 2,6-dichloro-4-nitrophenol were compared. The production of red alkaline solution by the two chloronitrophenols, and not by the first two compounds, was sufficient proof that 2-chloro-4-nitrophenol might have formed in the reaction, but was converted into other compounds by the excess of hypochlorous acid.

The oxidation product of the 2-chloro-4-nitrophenol was isolated, but not identified. It was incidentally isolated as a pyridine salt in an attempt to prepare the benzoic acid ester of the impure oxidation product, which was thought to be 2-chloro-4-nitrophenol.³ The quantity of the pyridine salt was rather

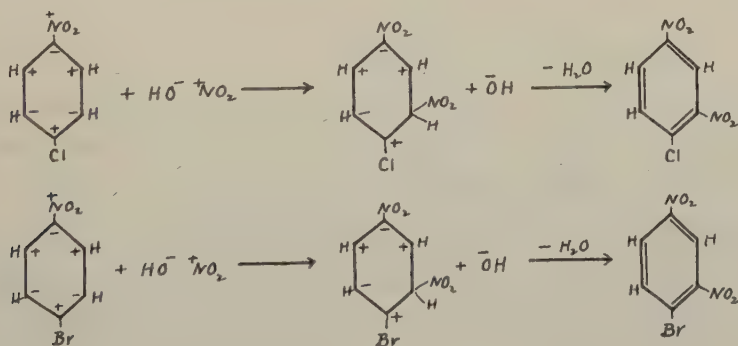
¹Müller, Jahr. u. Fort. der Chemie, 1873, 407.

²2,6-dichloro-4-nitrophenol is said to be oxidized by bromine water to dichloro-dibromo quinone, Ling, J. Chem. Soc., 51, 786; 61, 577.

³It may deserve mentioning that the benzoic acid ester of 2-chloro-4-nitrophenol is described in Beilstein, but the method of preparation was not given in the original article. The ester is best prepared by solution of the phenol in a small volume of

small. Taking it as a measure of the quantity of the 2-chloro-4-nitrophenol that might have formed as a first product through complete saturation of the Kekulé double bond, we may conclude that the introduction of the meta-orientating nitro group has also the unfavorable effect of diminishing the proportion of substitution product formed through complete saturation of the double bond in the aromatic nucleus--a fact similar to that observed in the nitration of p-nitrodimethylaniline and of p-nitroanisol.

The action of nitric acid on p-nitrochlorobenzene and on p-nitrobromobenzene was also briefly investigated. Since p-nitrochlorobenzene and p-nitrobromobenzene are less reactive compounds, the nitration was allowed to proceed in concentrated sulfuric acid solution at room temperature for a longer period of time. The reaction products isolated were exclusively 2,4-dinitrochlorobenzene¹ and 2,4-dinitrobromobenzene. They would be formed through absorption of the positive nitro group by the negative end of the Kekulé double bond.



pyridine and addition of an equivalent quantity of benzoyl chloride to the solution. This is warmed for five minutes, and the ester precipitated by dilution with water. The ester will easily decompose by longer contact with the alkaline solution.

¹H. Martinsen, Z. F. Phy. Chem., 59, 613 (1907).

No phenolic compound could be isolated, but by comparing the color of the alkaline solutions side by side with blank experiments, in which no nitric acid was used, there is some indication that a very small quantity of nitrophenol has been formed as a result of complete saturation of the double bond. The liberation of a small amount of hydrogen chloride on distilling the sulfuric acid solution filtrate may also be accounted for as the result of complete saturation. However, the quantity of the nitrophenol formed is in any event so small that we can only conclude, that the meta directing nitro group has an unfavorable effect on complete saturation, or, if to some slight extent complete saturation did take place, the removal of the chlorine and bromine atoms from the aromatic nucleus was so difficult, that complete saturation had the same result as if only the positive nitro group had been absorbed by one end of the Kekulé double bond.

The results of the series of experiments with the derivatives of nitrobenzene described above may be summarized as follows as regards their bearing on the Stieglitz theory of substitution in the benzene nucleus:

(1) In the action of nitrous and nitric acid on p-nitrodimethylaniline and p-nitroanisol the formation of phenols by the loss of dimethylamine and methyl alcohol, respectively, was proved in every case by the isolation and identification of their benzoic acid esters. In the other cases (hypochlorous acid on p-nitrodimethylaniline and p-nitroanisol, and nitric acid on p-nitrochlorobenzene and p-nitrobromobenzene), the formation of phenols was indicated by color reactions but the phenols were not isolated. The formation of phenols would follow complete addition of a reagent (HO^- and NO , NO_2 , Cl^+) to a Kekulé double bond in the

nucleus, the positive addendum joining to the relatively negative end of the double bond and negative OH to its positive end. It is the latter addition which would give the opportunity for the loss of dimethylamine or methyl alcohol, and hence the proved formation of the phenols is considered valid proof of such complete addition.

(2) The quantity of phenol obtained in any case is extremely small. This is taken as evidence that the chief substitution reaction is that of the uni-polar absorption of the positive addendum (NO^+ , NO_2^+ , Cl^+) by the negative end of the Kekulé double bond,¹ electrical neutrality and the aromatic nucleus being restored by the immediate loss of H^+ from the same carbon atom. Since the phenol formation showed clearly that the Kekulé double bonds are involved in the substitution reactions, it is altogether likely that they are also involved in the main substitution reaction, but the absorption limited to a single component of the addendum. Similar observations, it will be recalled, have been made in addition reactions of ordinary aliphatic double bonds.²

(3) The results indicate consistently that the presence of the nitro group reduces the amount of phenols obtained in these reactions. This is logically ascribed to the effect of the meta-directing strongly positive nitro group superimposed on the effect of the ortho-directing negative group ($\text{N}^-(\text{CH}_3)_2$, O^-CH_3 , etc.) in making the negative end of the Kekulé double bond relatively more strongly negative; the stronger negative field would favor the uni-polar absorption of the positive addendum in the way actually found to be the case.

¹Stieglitz, loc. cit., p. 1304.

²Terry and Eichelberger, loc. cit.

EXPERIMENTAL PART

I. Action of Nitrous Acid on p-Nitrodimethylaniline.

Para-nitrodimethylaniline was prepared by the action of fuming nitric acid on dimethylaniline dissolved in glacial acetic acid.¹ In order to get the pure product, the conditions must be very carefully regulated. After a dozen trials, the following procedure was used.

Dimethylaniline, fractionally distilled, was dissolved in eight times its volume of glacial acetic acid. The solution was cooled in ice, and colorless fuming nitric acid was added drop by drop to it. The quantity of the nitric acid added was 1 1/4 mole for 1 mole of dimethylaniline. The total volume of nitric acid should have been added before the reaction is allowed to take place. When all of the acid had been added, the mixture was immersed in warm water, shaken, and the increase in the temperature of the solution observed. At around 40° intense red drops began to form on the wall of the vessel. A drop of it, on flowing back to the solution mixture, started the nitration vigorously. The whole solution turned from red to blue and then yellow in a few seconds; simultaneously the temperature increased suddenly to 70°-80°. The solution was cooled immediately; p-nitrodimethylaniline separated as yellow shining crystals, and was collected on a filter after an hour. It was recrystallized once

¹Weber, Ber. 10, 761 (1877).

from benzene and then dissolved in a small volume of chloroform and precipitated fractionally by low-boiling ligroin. Pure yellow crystals, free from any blue or green tinge, melting at 163° , were obtained. It was found that improper regulation of the conditions leads to a blue or green discolored product, from which the colored impurity could not easily be removed by repeated recrystallization.

In the study of the action of nitrous acid on p-nitrodimethylaniline, the following solvents were used: chloroform, glacial acetic acid, dilute hydrochloric acid, and dilute sulfuric acid. The first one, chloroform, gave results somewhat different from the latter three.

A. In Chloroform:--Six experiments were performed upon the reaction of nitrous acid on p-nitrodimethylaniline in chloroform. The best result was obtained in the following way. Twelve grams of p-nitrodimethylaniline was dissolved in 200 cc. of chloroform, and 16 g. of powdered sodium nitrite added. The whole was cooled in ice, and 50 cc. of 6-N hydrochloric acid added drop by drop, from a separatory funnel, with mechanical stirring. This addition of hydrochloric acid took place in four hours. Stirring was continued for another two hours, and then a current of hydrogen was passed through the mixture to displace the excess of nitrogen oxide. Still being kept in ice, the mixture was made alkaline by the slow addition of 5% sodium carbonate solution.¹ The chloroform layer was then separated from the

¹The use of weak alkali was necessary in order to avoid the decomposition of the 2,4-dinitrodimethylaniline which is formed in this reaction. It is stated in the literature (K. H. Mertens, *Ber.* 19, 2124 [1886]) that 2,4-dinitrodimethylaniline will be decomposed by warming with sodium hydroxide solution, giving 2,4-dinitrophenol and dimethylamine. This was confirmed, and it was also found that even on standing of the alkaline mixture at room temperature, the 2,4-dinitrodimethylaniline would be slowly decomposed. Sodium carbonate will not decompose 2,4-dinitrodimethylaniline at room temperature.

aqueous alkaline solution, and was again shaken twice with 5% sodium carbonate. It was dried over anhydrous sodium sulfate. The alkaline aqueous solution and extracts were combined and shaken with a small quantity of fresh chloroform¹ to remove any non-phenolic substances that may have entered into the aqueous solution.

The chloroform solution, dried over anhydrous sodium sulfate, was evaporated. The golden yellow residue weighed approximately 14 g. after being dried in vacuo. Upon recrystallization twice from methyl alcohol, the compound was found to have a melting point of 87°. It was identified as 2,4-dinitrodimethylaniline, by the melting point of the mixture with known 2,4-dinitrodimethylaniline, prepared by direct nitration of dimethylaniline.²

The alkaline aqueous solution, orange in color, was acidified with hydrochloric acid, and the light yellow colored solution extracted four times with ether. After being dried over anhydrous sodium sulfate over night, the ether extract was evaporated at a low temperature. Yellow colored crystals mixed with some gummy substances were obtained. The whole mixture weighed approximately 20 milligrams. Nitrophenol crystals were partially separated from the gummy substances by extraction with a little chloroform, in which the gummy substance was less soluble. After removal of the chloroform, the nitrophenol was converted into its benzoic acid ester by being heated with 2

¹The use of chloroform was preferable to ether because p-nitrodimethylaniline and 2,4-dinitrodimethylaniline are much more soluble in chloroform than in ether.

²Mertens, Ber., 19, 2123 (1886).
Finnow, Ber., 32, 1666 (1899).

drops of benzoyl chloride.¹ The tiny amount of benzoic acid ester was recrystallized by the addition of low boiling ligroin to the chloroform solution. Filtration was performed in a specially made glass ground joint micro-filtering tube. The ester was a little yellowish in color, m.p. 130°. It was identified as the benzoate of 2,4-dinitrophenol by the melting point of a mixture of the compound and some of the synthetic ester.

A color reaction was also used to identify the phenol as 2,4-dinitrophenol. Differing from the mono-nitrophenols, 2,4-dinitrophenol does not give a ferric chloride color reaction in acidic solution. On the addition of sodium carbonate solution, a pink color developed before the precipitation of ferric hydroxide.

In order to show that the 2,4-dinitrophenol was formed as a result of the direct action of nitrous acid on p-nitrodimethylaniline, and not from other secondary means, the following blank tests were performed:

When p-nitrodimethylaniline was treated as above, omitting the use of sodium nitrite, no nitrophenol was produced. The aqueous alkaline layer remained colorless after being shaken with chloroform.

When 2,4-dinitrodimethylaniline was treated as above, omitting the use of sodium nitrite, no nitrophenol was produced.

B. In Glacial Acetic Acid:--p-Nitrodimethylaniline is not easily soluble in glacial acetic acid, but it readily dissolves on the addition of a small volume of concentrated hydrochloric acid. Four experiments were performed to study the action of nitrous acid on p-nitrodimethylaniline, in glacial acetic acid

¹Kym, Ber., 32, 1427 (1899).

as solvent.

Twelve grams of p-nitrodimethylaniline was stirred in 150 cc. of glacial acetic acid, and 40 cc. of concentrated hydrochloric acid diluted with 20 cc. water was added, whereby a homogeneous solution resulted. It was cooled well in ice water and solid sodium nitrite added to it with vigorous stirring. In the course of four hours, fifteen grams of sodium nitrite was added. A bulky yellow precipitate separated. After one more hour of stirring, the yellow precipitate was collected on a filter, and the filtrate (X) reserved for further examination.

The yellow solid, dried over calcium chloride in vacuo, was extracted with chloroform to remove the sodium chloride and any unchanged sodium nitrite. After evaporation of the chloroform, the residue weighed ten grams. It was recrystallized twice from carbon tetrachloride and twice from a chloroform-ligroin combination (a benzene-ligroin combination can also be used). Nearly colorless crystals, m.p. 101°, were finally obtained.

The compound was identified as N-nitroso-p-nitro-monomethylaniline; it gave the diphenyl amine test for a nitrosamine;¹ and on being boiled with concentrated hydrochloric acid, it was hydrolyzed to p-nitromonomethylaniline hydrochloride; when the latter solution was made alkaline, the free amine was precipitated. Recrystallization from a chloroform-ligroin combination gave pure yellow crystals of p-nitromonomethylaniline,² m.p. 152°.

¹Mulliken, "Identification of Pure Organic Compounds," II, 27.

²Stoermer and Hoffmann, Ber. 31, 2529 (1898).

Analysis¹ of the N-nitroso-p-nitromonomethylaniline:

Weight of sample	4.302 mg.
Vol. of N ₂ , corrected	0.886 cc.
Pressure, corrected	735.6 mm.
Temperature	25°
Percentage of N	22.9%
Theoretical for C ₇ H ₇ O ₃ N ₃	23.2%

Through the filtrate (X) (see above) hydrogen was bubbled to displace most of dissolved nitrogen oxides. On dilution with two volumes of water, more of the pale yellow precipitate separated out, and was identified as N-nitroso-p-nitromonomethylaniline; the filtrate was then well cooled, and solid sodium carbonate added to it slowly, with stirring. A yellow precipitate was formed. After the solution reacted alkaline, it was filtered. The yellow precipitate dried, was extracted with chloroform and reprecipitated with low boiling ligroin. About half a gram of a pale yellow substance was obtained which on recrystallization from carbon tetrachloride, was identified as N-nitroso-p-nitromonomethylaniline.

The alkaline sodium acetate solution filtrate was shaken with chloroform to remove any non-phenolic substances dissolved in it, and was then allowed to evaporate spontaneously to a smaller volume. After separation from the sodium acetate that crystallized on concentrating, the filtrate was cooled and made acid with sulfuric acid. Filtration removed the sodium sulfate and the solution was extracted five times with ether. The yellow ether solution was allowed to evaporate spontaneously, leaving behind an acetic acid solution of a nitrophenol. Distillation of

¹Analyses were carried out by the Pregl microchemical methods.

the acetic acid, or evaporation over sodium hydroxide in vacuo would cause the volatilization of the nitrophenol;¹ the acetic acid solution was therefore treated with ethyl alcohol and the mixture distilled. The ethyl alcohol was added in portions as long as ethyl cetate was passing over. After this irreversible removal of acetic acid, the distillation was continued further to remove most of the ethyl alcohol. An aqueous solution of nitrophenol was thus obtained. After extraction with ether and evaporation of the extract, a residue in very small amount with white crystals was obtained. It was impossible to take a melting point, and to transform it into benzoic acid ester. It did give the color reactions of 2,4-dinitrophenol.

C. In Dilute Hydrochloric Acid or Sulfuric Acid:--More experiments were performed with dilute hydrochloric acid as the solvent, but it was later found that dilute sulfuric acid gave better results. With hydrochloric acid as the solvent, more tarry substance was obtained. Only the reaction in sulfuric acid solution will be described.

Five grams of p-nitrodimethylaniline was dissolved in 80 cc. of dilute sulfuric acid (1:5) and the solution was well cooled. Small portions of solid sodium nitrite were added at intervals during four hours. A total of 5.6 g. was added. During the addition of the sodium nitrite, a yellow precipitate separated gradually. After six hours, the yellow precipitate was collected. Recrystallized, it was identified as N-nitroso-p-nitrodimethylaniline. The crude product weighed 4.5 grams.

The sulfuric acid filtrate was diluted with an equal

¹Tested with known 2,4-dinitrophenol. The removal of acetic acid by neutralization and extraction was also impracticable, since 2,4-dinitrophenol ($K_i = 1 \times 10^{-4}$) is a stronger acid than acetic acid ($K_i = 1.8 \times 10^{-5}$).

volume of water, whereby some yellow precipitate separated. After filtration, the filtrate (Y) was subjected to further examination according to the next paragraph. The residue was dried, recrystallized twice from methyl alcohol, and was identified as 2,4-dinitrodimethylaniline. It weighed less than half a gram.

The filtrate (Y) (see above), light yellow in color, was extracted four times with ether, and the combined ether extract shaken with 5% sodium carbonate solution. The alkaline solution became orange yellow in color. In order to remove any non-phenolic substances that may have entered into the aqueous solution, the alkaline extract was shaken once with chloroform. After separation of the latter, the alkaline extract was acidified with dilute hydrochloric acid. The acidified solution, pale yellow in color, was then extracted four times with ether. After being dried over anhydrous sodium sulfate, the ether extract was evaporated at a low temperature.

The residue from ether, though it weighed less than two-hundredths of a gram, contained a nitrophenol in purer form than previously obtained. The contamination with tar was less. It was purified once by extraction with chloroform, and converted into its benzoic acid ester by the Schotten-Baumann's reaction, which gave a better product than the method previously used. The crude nitrophenol, contained in a small test tube, was dissolved in eight drops of pyridine, and two small drops of benzoyl chloride were added to the solution. After standing for ten minutes, not longer, the solution was diluted with water, shaken to effect coagulation, cooled, and filtered without much delay. The crystals gave the melting point 131° . The melting point remained unchanged when the ester was mixed with a known specimen of the benzoic acid ester of 2,4-dinitrophenol. This identified

the nitrophenol as 2,4-dinitrophenol.

In order to follow the mechanism for the formation of the N-nitroso-p-nitromonomethylaniline, a test for the simultaneous formation of formaldehyde (see p. 15) was made. In one of the experiments, the hydrochloric acid filtrate, after the removal of N-nitroso-p-nitromonomethylaniline, was used. Four cc. of it was made alkaline with sodium carbonate, the solution filtered, and the resorcinol test applied.¹ A deep red solution was formed on boiling, the same as formed with a known formaldehyde solution. To another portion of the hydrochloric acid solution, the guaiacol ring test² was applied. The result was identical with that obtained with a known formaldehyde solution. Nitrous acid gives a ring, but of a different color.

II. Action of Hypochlorous Acid on p-Nitrodimethylaniline.

The hypochlorous acid used was prepared according to the method described in Muskat's paper.³ Its strength was determined by titration with potassium iodide and sodium thiosulfate, immediately before its use. It was around 2-molar.

Five experiments were performed upon the reaction of hypochlorous acid on p-nitrodimethylaniline. The p-nitrodimethylaniline (8 grams) was suspended in 100 cc. of carbon tetrachloride, the mixture well cooled in ice and one mole equivalent of hypochlorous acid added to it with vigorous stirring. After an hour all the p-nitrodimethylaniline had reacted with the hypochlorous acid, as was indicated by the solution of the nitrodimethylaniline in carbon

¹Rosenthaler, "Nachweis organischer Verbindungen," p. Lebbin, Centralblatt, 1897 I, 270.

²H. Meyer, "Nachweis und Bestimmung organischer Verbindungen," Bd II, 47.

³I. E. Muskat, Doctorate Dissertation, University of Chicago, 1927, p. 47.

tetrachloride. The stirring was continued for another hour, and then the aqueous solution was separated from the carbon tetrachloride solution.

The aqueous solution was carefully made alkaline by a 5% sodium carbonate solution; it became blood-red. The carbon tetrachloride solution was repeatedly extracted with 5% sodium carbonate solution; more than ten extractions were necessary. The alkaline extracts were also blood-red in color, very intense in the first extract. The formation of the red color was not instantaneous, as by the action of alkali on nitrophenols. It appeared gradually when the mixtures were shaken. That the formation of the red colored solution was not due to the action of oxygen in the air was shown by the fact that the same result was obtained by stirring the carbon tetrachloride solution with alkali in a closed vessel through which a current of hydrogen was passing. The alkaline solution and the extracts were combined (Z).

The carbon tetrachloride solution was dried, concentrated, and low boiling ligroin was added to it. There separated out yellow crystals which weighed approximately 7 grams. The substance was recrystallized by precipitation with low boiling ligroin from its solution in benzene. After two recrystallizations, it gave the melting point 78° . It was identified as 2-chloro-4-nitrodimethylaniline.¹

Analysis for chlorine:

Weight of sample	5.273 mg.	5.005 mg.
Weight of AgCl	3.800 mg.	3.617 mg.
% of Cl found	17.83%	17.88%
% of Cl theoretical for $C_8H_9O_2N_2Cl$		17.68%

The red colored alkaline solution (Z) (see above) was

¹Van Duin, Rec. trav. chim., 51, 878 (1932), by nitration of o-chloro-dimethylaniline.

acidified with hydrochloric acid and extracted five times with ether. The ether solution, dried and evaporated, left a tarry residue with some crystals, which were partially purified by extraction with chloroform. On evaporation of the chloroform, the residue weighed only twelve milligrams. An attempt was made to convert it into an ester, pyridine being used as a solvent. It was, however, found that the crude product reacted with pyridine (2-chloro-4-nitrophenol and 2,6-dichloro-4-nitrophenol are both soluble in pyridine, and can be reprecipitated unchanged by dilution with water), forming a yellow precipitate which was insoluble in benzene but soluble in alcohol and water. It melted around 170° , but it was impossible to purify and analyze it. Probably it was a pyridine salt of some chloro-nitrophenol of strong acid strength. The yellow aqueous solution when shaken with strong alkali, liberated pyridine. On acidification, the solution was decolorized.

The failure to isolate the chloronitrophenol is probably due to the reactivity of the 2-chloro-4-nitrophenol first formed with hypochlorous acid. The following experiment was performed to show this to be the case.

2-Chloro-4-nitrodimethylaniline, 2-chloro-4-nitrophenol and 2,6-dichloro-4-nitrophenol, each dissolved in carbon tetrachloride, were simultaneously shaken for two hours with an excess of hypochlorous acid. When the mixtures are made alkaline and shaken, the two chloronitrophenols gave red aqueous layers, but the 2-chloro-4-nitrodimethylaniline gave only a pale yellow aqueous solution.

The action of a dilute sodium carbonate solution on 2-chloro-4-nitrodimethylaniline was also studied. On being shaken and on standing at room temperature, the 2-chloro-4-nitrodimethylaniline was not hydrolyzed. But a sodium hydroxide

solution hydrolyzed the compound to give a yellow solution of 2-chloro-4-nitrophenol under similar conditions.

III A. Action of Nitrous Acid on p-Nitroanisol.

p-Nitroanisol, recrystallized from methyl alcohol, was dissolved in chloroform and treated with sodium nitrite and hydrochloric acid, in the same way as used with p-nitrodimethylaniline. The p-nitroanisol was not attacked even after 12 hours of stirring. No reaction occurred either when glacial acetic acid was used as the solvent.

III B. Action of Nitric Acid on p-Nitroanisol.

p-Nitroanisol was also stable toward nitric acid when glacial acetic acid was used as the solvent. One gram of p-nitrophenol was dissolved in 12 cc. of glacial acetic acid, and treated with 12 cc. of concentrated nitric acid. The solution was heated at 90° for 4 hours, but the p-nitrophenol was recovered unchanged. Neither dinitroanisol nor nitrophenol could be isolated. Concentrated sulfuric acid was finally used as the solvent.

p-Nitroanisol, 10 grams, was dissolved in 150 cc. of cold concentrated sulfuric acid (sp. gr. 1.84). Ten cc. of concentrated nitric acid (sp. gr. 1.42) was added to the solution. After standing in ice water for an hour, it was poured slowly on ice, with stirring. The precipitate was collected on the filter, and the filtrate (W_2) reserved for further examination.

The precipitate, after being dried, was dissolved in ether, and the ether solution extracted twice with 5% sodium carbonate solution. The combined sodium carbonate solution (W_2), yellow in color, was extracted once with a little ether to remove any non-phenolic substances, and was reserved for use later. The main ether solution was evaporated at low temperature. Impure 2-4-dinitroanisol was obtained, weighing approximately 10 grams. After

recrystallization twice from methyl alcohol, it melted sharply at 87°. There was no change in the melting point after the compound was mixed with 2,4-dinitroanisol prepared by other methods.¹

The sulfuric acid filtrate (W₁) was extracted four times with ether, and the combined ethereal solutions extracted three times with 5% sodium carbonate solution. This alkaline solution was then extracted once with ether to remove any non-phenolic substances, and combined with the previous sodium carbonate solution (W₂). After acidification with hydrochloric acid, the nitrophenol that was set free, was extracted thoroughly with ether. On evaporation of the ether, pale yellow crystals were obtained, mixed with some tarry substances. The mixture weighed approximately 30 milligrams.

The nitrophenol was extracted with chloroform, and the chloroform solution evaporated in a small test tube. The nitrophenol was converted into its benzoic acid ester by being heated with benzoyl chloride for one hour at 185°. After purification by being briefly warmed with dilute ammonium hydroxide, it was collected, dried and recrystallized by solution in chloroform and precipitation with low boiling ligroin. It formed pale yellow crystals, m.p. 130°. When mixed with a known benzoic acid ester of 2,4-dinitrophenol, m.p. 131°, it melted at 130.5°.

In order to show that the 2,4-dinitrophenol was obtained as the result of direct nitration of p-nitroanisol, the following experiments were performed.

When an ethereal solution of p-nitroanisol was shaken with 5% sodium carbonate solution, the sodium carbonate solution was not colored.

When an ethereal solution of 2,4-dinitroanisol was shaken

¹Holleman, Rec. trav. chim., 22, 270 (1903).
Meldola, Woolcott, and Wray, J. Chem. Soc., 69, 1330 (1896).

with 5% sodium carbonate solution, the sodium carbonate solution was not colored.¹

One gram of p-nitroanisol was dissolved in cold concentrated sulfuric acid; the solution was poured on ice after standing for an hour. When the filtrate is made alkaline, it did not give any yellow color.

Similarly 2,4-dinitroanisol was found not to be decomposed into 2,4-dinitrophenol on solution in concentrated sulfuric acid.

IV. Action of Hypochlorous Acid on p-Nitroanisol.

p-Nitroanisol, 8 grams, was dissolved in 40 cc. of carbon tetrachloride, and the solution shaken with a mole equivalent of hypochlorous acid for 24 hours. The aqueous layer was made alkaline, thus producing a blood-red colored solution, the same as in the case of the action of hypochlorous acid on p-nitrodimethylaniline. The carbon tetrachloride solution was shaken with 5% sodium carbonate solution. The extraction was repeated until the alkaline layer became only light yellow-colored. All the alkaline extracts were then combined (Q), and shaken once with a little fresh carbon tetrachloride to remove any nitroanisol that might have passed into the aqueous solution.

The carbon tetrachloride solution was evaporated. The residue, weighing about seven grams, was fractionally recrystallized from methyl alcohol. Two kinds of crystals were obtained, one melting at 45°-50°, and the other melting at 85°-90°. The low melting compound was further recrystallized from methyl alcohol, and was identified as unchanged p-nitroanisol, melting at 54°. The high melting compound was recrystallized by solution in benzene and precipitation by low boiling ligroin. It formed white fibery crystals, and was identified as 2-chloro-4-nitroanisol, melting at 92.5

¹Sodium hydroxide will slowly hydrolyze 2,4-dinitroanisol.

Analysis for Chlorine:

Weight of sample	5.502 mg.
Weight of AgCl	4.442 mg.
% of Cl found	18.97%
Theoretical for $C_7H_6O_3NCl$	18.91%

The blood-red aqueous alkaline solution (Q) was treated in the same way as described under the action of hypochlorous acid on p-nitrodimethylaniline. The tarry residue gave similarly with pyridine a yellow compound insoluble in benzene. It also could not be recrystallized.

The fact that the red colored alkaline solution, and the yellow pyridine salt were due to the action of hypochlorous acid on 2-chloro-4-nitrophenol and not due to the decomposition of 2-chloro-4-nitroanisol, was proved by shaking 2-chloro-4-nitroanisol with hypochlorous acid for two hours. This experiment was performed in conjunction with that on 2-chloro-4-nitro dimethyl aniline. When the mixture was made alkaline, the aqueous layer remained colorless.

V. Action of Nitric Acid on p-Nitrochlorobenzene and on p-Nitrobromobenzene.

p-Nitrochlorobenzene and p-nitrobromobenzene are still less readily acted on by nitric acid. Concentrated sulfuric acid was used as the solvent, and the reaction was allowed to proceed at room temperature.

p-Nitrochlorobenzene, 10 g., was dissolved in cold concentrated sulfuric acid (sp. gr. 1.84), and 7 cc. of concentrated nitric acid (sp. gr. 1.42) was added to the solution. The mixture was allowed to stand over night and then poured on ice. The white precipitate was collected, dried, dissolved in not too small a volume of chloroform, and precipitated with low boiling

ligroin. White crystals were obtained, m.p. 50°. The 2,4-dinitrochlorobenzene¹ may also be recrystallized from carbon tetrachloride, or by solution in benzene and precipitation with low boiling ligroin.

Analysis for Chlorine:

Weight of sample	4.283 mg.
Weight of AgCl	3.023 mg.
% of Cl found	17.46%
Theoretical for $C_6H_5O_4N_2Cl$	17.51%

The aqueous sulfuric acid solution filtrate was extracted four times with ether for phenolic substances, and the combined ether extract shaken three times with 5% sodium carbonate solution. The alkaline extract was orange yellow. On acidification and extraction with ether, only a small amount of tarry substances mixed with some crystals was obtained. Conversion of the nitrophenol into a benzoic acid ester was not successful.

In another experiment, starting also with 10 g. of p-nitrochlorobenzene, the concentrated sulfuric acid solution was poured slowly into ice-cold distilled water, and the filtrate distilled. Silver nitrate gave a distinct turbidity to the distillate. A blank, in which p-nitrochlorobenzene was used but the nitric acid omitted, gave a distillate free from chloride ion.

Three further control mixtures were made under the same conditions:

- (1) p-Nitrochlorobenzene + H_2SO_4 + HNO_3
- (2) p-Nitrochlorobenzene + H_2SO_4
- (3) 2,4-Dinitrochlorobenzene + H_2SO_4 .

After standing over night, the mixtures were poured on ice, and

¹Einhorn, Frey, Ber., 27, 2457.

the color of the filtrates compared after they were made alkaline. They were all yellow, but this was more intense in the first case. This showed that a little of some nitrophenol did form by the action of nitric acid on p-nitrochlorobenzene. The yellow color of the latter two solutions was probably due to a slight sulfonation of the p-nitrochlorobenzene.

The action of nitric acid on p-nitrobromobenzene was studied in the same way. 2,4-Dinitrobromobenzene¹ was the main product formed. It was recrystallized from ethyl alcohol, forming white plates, m.p. 72°.

Analysis for bromine:

Weight of sample	4.946 mg.
Weight of AgBr	3.781 mg.
% of Br found	32.6%
Theoretical for $C_6H_3O_4N_2Br$	32.4%

The alkaline extract was light yellow. On acidification and extraction with ether, only a very small amount of residue was obtained, but it did show color reactions of nitrophenols.

Three control mixtures were also made under the same conditions:

- (1) p-Nitrobromobenzene + H_2SO_4 + HNO_3
- (2) p-Nitrobromobenzene + H_2SO_4
- (3) 2,4-Dinitrobromobenzene + H_2SO_4

The resulting aqueous filtrates, after being made alkaline, were all yellow, being slightly deeper colored in the first mixture.

¹Kekulé, Ann., 137, 167 (1866).

SUMMARY

1. A series of experiments was carried out upon the action of nitrous acid, nitric acid, and hypochlorous acid on aromatic nitro compounds in order to obtain further evidence bearing on the Stieglitz theory of substitution reactions in the benzene series, and in particular in order to study the effect of the nitro group on the extent of one of the two possible procedures in the mechanism according to the theory.

2. The action of nitrous acid on p-nitrodimethylaniline was carried out in four different solvents--glacial acetic acid, dilute hydrochloric acid, dilute sulfuric acid, and chloroform. 2,4-Dinitrophenol was isolated and its benzoic ester prepared and identified in the case of the last two solvents. The same compound was isolated and recognized by its color reactions, when the first two solvents were used. The 2,4-dinitrophenol can only be formed by complete saturation of the Kekulé double bond, one of the two possible procedures in the mechanism of substitution in aromatic nucleus according to the Stieglitz theory. In every case the quantity of 2,4-dinitrophenol obtained was very small. This is considered evidence that complete saturation of the Kekulé double bond takes place only to a very minor extent.

3. 2,4-Dinitrodimethylaniline was isolated as the major product in the above reaction when chloroform was used as the solvent. It was formed as the result of uni-polar absorption of the positive nitroso group by the negative end of the Kekulé double bond, an alternative procedure in the mechanism of

substitution according to the theory. The result indicates that uni-polar absorption is the chief mechanism of nuclear substitution in this reaction.

4. When glacial acetic acid, dilute hydrochloric acid, or dilute sulfuric acid was used as the solvent, N-nitroso-p-nitromonomethylaniline was the chief compound formed in the above reaction. It is the product of the action of nitrous acid on the p-nitrodimethylphenylammonium ion $[\text{NO}_2\text{-C}_6\text{H}_4\text{-N}(\text{CH}_3)_2\text{H}^+]$, formed in acid solutions. In chloroform solution, that is in the absence of a strong acid, the nuclear substitution product, 2,4-dinitrodimethylaniline is the major product. The results show convincingly that an extra-nuclear reaction is not at all necessary for nuclear substitution, as some chemists hold, and that extra-nuclear substitution, when it does take place, is simply the result of the greater reactivity of the extra-nuclear group--in the present instance an NH group.

5. By the action of nitric acid on p-nitroanisol in concentrated sulfuric acid solution, 2,4-dinitrophenol was also isolated and identified through its ester. It was formed through complete saturation of the Kekulé double bond. The major compound isolated was 2,4-dinitroanisol. The theoretical bearings of these findings are exactly the same as given above.

6. The chlorination of p-nitrodimethylaniline by hypochlorous acid gave 2-chloro-4-nitrodimethylaniline as the main product. 2-Chloro-4-nitrophenol, whose formation is suggested by the theory, could not be isolated on account of its reactivity toward hypochlorous acid; but there is strong evidence based on color reactions that it was formed.

7. The same result was obtained in the chlorination of p-nitroanisol by hypochlorous acid. 2-Chloro-4-nitroanisol was

the main product. It was also not possible to isolate the 2-chloro-4-nitrophenol, but its transient formation has also been verified by color reactions.

8. p-Nitrochlorobenzene and p-nitrobromobenzene were also nitrated by nitric acid in concentrated sulfuric acid solution. 2,4-Dinitrochlorobenzene and 2,4-dinitrobromobenzene were formed exclusively. The colors produced in the color reactions of the nitrophenol that may have been formed, are only comparative.

9. The identification of substituted phenols as products of the action by the isolation of its benzoic acid ester (see paragraphs 2 and 5) and the color reactions (see paragraphs 2, 6, 7 and 8) is evidence of complete saturation of a Kekulé double bond. But their formation in very small quantities is proof that complete saturation of Kekulé double bond is only a very minor part of the action. Since such phenols are formed to a far greater extent in the absence of the nitro group (Cf. particularly Hoffman's work, loc. cit., on anisol), it is evident that the introduction of the strong meta directing nitro group $^+\text{NO}_2$ is a factor acting as a deterrent to complete saturation of a Kekulé double bond. Substitution results rather from uni-polar addition of a positive addendum (^+NO , $^+\text{NO}_2$, Cl^+) to the negative end of such a double bond with practically simultaneous loss of H^+ . It is suggested that the introduction of the nitro group favors this form of substitution because the effect of the strongly positive nitro group in position 4 is superimposed on the effect of the negative group in position 1 to make position 2 decidedly negative.

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